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**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:  
Elmer M. Price

Serial No.: 10/808,248

Filed: March 24, 2004

For: METHOD OF TREATMENT OF  
ENDOTHELIAL DYSFUNCTION AND  
ENGINEERED PROTEINS FOR SAME

Group Art Unit: 1614

Examiner: Unknown

Atty. Dkt. No.: UVMO:024US

CERTIFICATE OF MAILING 37 C.F.R. 1.8	
I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: MS AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:	
January 12, 2005	
Date	Steven L. Highlander

**INFORMATION DISCLOSURE STATEMENT**

**MS AMENDMENT**

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

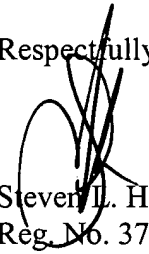
In accordance with 37 C.F.R. §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be

an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R. § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/UVMO:024US.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,



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Date: January 12, 2005

Form PTO-1449 (modified)

Atty. Docket No.

UVMO:024US

Serial No.

10/808,248

List of Patents and Publications for Applicant's

Applicant

Elmer M. Price *et al.*

INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

Filing Date:

March 24, 2004

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U.S. Patent Documents

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Foreign Patent Documents

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Other Art

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## U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.

## Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No

## Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

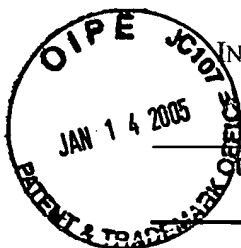
Exam. Init.	Ref. Des.	Citation
	C1	Alexander <i>et al.</i> , "Gene transfer of endothelial nitric oxide synthase but not Cu/Zn superoxide dismutase restores nitric oxide availability in the SHRSP," <i>Cardiovascular Res.</i> , 47:609-617, 2000.
	C2	Bachmair <i>et al.</i> , "The degradation signal in a short-lived protein," <i>Cell</i> , 56:1019-1032, 1989.
	C3	Bivalacqua <i>et al.</i> , "Adenoviral gene transfer of endothelial nitric oxide synthase (eNOS) to the penis improves age-related erectile dysfunction in the rat," <i>Intl. J. Impotence Res.</i> , 12 Suppl 3:S8-17, 2000.
	C4	Cable <i>et al.</i> , "Expression and function of a recombinant endothelial nitric oxide synthase gene in porcine coronary arteries," <i>Cardiovascular Res.</i> , 35(3):553-559, 1997.
	C5	Cable <i>et al.</i> , "Recombinant endothelial nitric oxide synthase-transduced human saphenous veins: gene therapy to augment nitric oxide production in bypass conduits," <i>Circulation</i> , 96(9 Suppl.):II173-178, 1997.
	C6	Calles- Escandon and Cipolla, "Diabetes and endothelial dysfunction: a clinical perspective," <i>Endocrine Reviews</i> , 22:36-52, 2001.
	C7	Darbinian <i>et al.</i> , "Growth inhibition of glioblastoma cells by human Pur(alpha)," <i>J. Cell. Physiol.</i> , 189:334-340, 2001.
	C8	De Vriese <i>et al.</i> , "Endothelial dysfunction in diabetes," <i>British J. Pharmacol.</i> , 130:963-974, 2000.

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Form PTO-1449 (modified)		Atty. Docket No. UVMO:024US	Serial No. 10/808,248
List of Patents and Publications for Applicant's  INFORMATION DISCLOSURE STATEMENT  (Use several sheets if necessary)		Applicant Elmer M. Price <i>et al.</i>	
		Filing Date: March 24, 2004	Group: 1614
U.S. Patent Documents <i>See Page 1</i>	Foreign Patent Documents <i>See Page 1</i>	Other Art <i>See Page 1</i>	

### Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C9	Ferrario <i>et al.</i> , "The hypertension-lipid connection: insights into the relation between angiotensin II and cholesterol in atherogenesis," <i>Amer. J. Med. Sciences</i> , 323:17-24, 2002.
	C10	Forstermann <i>et al.</i> , "Isoforms of nitric-oxide synthase: purification and regulation," <i>Methods Enzymology</i> , 233:258-265, 1994.
	C11	Frankel and Pabo, "Cellular uptake of the tat protein from human immunodeficiency virus," <i>Cell</i> , 55:1189-1193, 1988.
	C12	Frankel <i>et al.</i> , "Dimerization of the tat protein from human immunodeficiency virus: a cysteine-rich peptide mimics the normal metal-linked dimer interface," <i>Proc. Natl. Acad. Sci., USA</i> , 85(17):6297-6300, 1988.
	C13	Frankel <i>et al.</i> , "Tat protein from human immunodeficiency virus forms a metal-linked dimer," <i>Science</i> , 240:70-73, 1988.
	C14	Garcia <i>et al.</i> , "Functional domains required for tat-induced transcriptional activation of the HIV-1 long terminal repeat," <i>EMBO J.</i> , 7(10):3143-3147, 1988.
	C15	Guerci <i>et al.</i> , "Endothelial dysfunction and type 2 diabetes. Part 1: physiology and methods for exploring the endothelial function," <i>Diabetes Metab.</i> , 27(4pt1):425-434, 2001.
	C16	Guerci <i>et al.</i> , "Endothelial dysfunction and type 2 diabetes. Part 2: altered endothelial function and the effects of treatments in type 2 diabetes mellitus," <i>Diabetes Metab.</i> , 27:436-447, 2001.
	C17	Han <i>et al.</i> , "Efficient intracellular delivery of GFP by homeodomains of Drosophila Fushi-tarazu and Engrailed proteins," <i>Molecules and Cells</i> , 10:728-732, 2000.
	C18	Hauber <i>et al.</i> , "Mutational analysis of the conserved basic domain of human immunodeficiency virus tat protein," <i>J. Virol.</i> , 63:1181-1187, 1989.
	C19	Hingorani, "Polymorphisms in endothelial nitric oxide synthase and atherogenesis," <i>Atherosclerosis</i> , 154:52 1-527, 2000.
	C20	Jain <i>et al.</i> , "Enalapril acts through release of nitric oxide in patients with essential hypertension," <i>Renal Failure</i> , 23(5):651-657, 2001.
	C21	Jin <i>et al.</i> , "Transduction of human catalase mediated by an HIV-1 TAT protein basic domain and arginine-rich peptides into mammalian cells," <i>Free Rad. Biol. Med.</i> , 31(11):1509-1519, 2001.

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Exam. Init.	Ref. Des.	Citation
	C22	Kwon <i>et al.</i> , "Transduction of Cu,Zn-superoxide dismutase mediated by an HIV-1 Tat protein basic domain into mammalian cells," <i>FEBS Letters</i> , 485:163-167, 2000.
	C23	Leber <i>et al.</i> , "Characterization of recombinant human endothelial nitric-oxide synthase purified from the yeast <i>Pichia pastoris</i> ," <i>J. Biol. Chem.</i> , 274:37658-37664, 1999.
	C24	Lin <i>et al.</i> , "Prolonged reduction of high blood pressure with human nitric oxide synthase gene delivery," <i>Hypertension</i> , 30(3pt1):307-313, 1997.
	C25	Lopez Farre and Casado, "Heart failure, redox alterations, and endothelial dysfunction," <i>Hypertension</i> , 38:1400-1405, 2001.
	C26	Luscher, "Vascular protection: current possibilities and future perspectives," <i>IJCP Supplement</i> , 117:3-6, 2001.
	C27	Maeso <i>et al.</i> , "Effect of atorvastatin on endothelium-dependent constrictor factors in dyslipidemic rabbits," <i>General Pharmacol.</i> , 34(4):263-272, 2000.
	C28	Monacada <i>et al.</i> , "The L-arginine-nitric oxide pa," <i>New Engl. J. Med.</i> , 329:2002-2012, 1993.
	C29	Nagahara <i>et al.</i> , "Transduction of full-length TAT fusion proteins into mammalian cells: TAT-p27Kip1 induces cell migration," <i>Nature Medicine</i> , 4:1449-1452, 1998.
	C30	Olsen <i>et al.</i> , "Endothelial dysfunction in resistance arteries is related to high blood pressure and circulating low density lipoproteins in previously treated hypertension," <i>Amer. J. Hypertension</i> , 14(9pt1):861-867, 2001.
	C31	Qian <i>et al.</i> , "Nitric oxide synthase gene therapy rapidly reduces adhesion molecule expression and inflammatory cell infiltration in carotid arteries of cholesterol-fed rabbits," <i>Circulation</i> , 99:2979-2982, 1999.
	C32	Ruben <i>et al.</i> , "Structural and functional characterization of human immunodeficiency virus tat protein," <i>J. Virology</i> , 63:1-8, 1989.
	C33	Sadaie <i>et al.</i> , "Human immunodeficiency virus type 1 rev protein as a negative trans-regulator," <i>DNA</i> , 8(9):669-674, 1989.
	C34	Schwarze <i>et al.</i> , "In vivo protein transduction: delivery of a biologically active protein into the mouse," <i>Science</i> , 285:1569-1572, 1999.
	C35	Schwarze <i>et al.</i> , "In vivo protein transduction: intracellular delivery of biologically active proteins, compounds and DNA," <i>Trends in Pharmacol. Science</i> , 21:45-48, 2000.

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	C36	Suwaiddi <i>et al.</i> , "Long-term follow-up of patients with mild coronary artery disease and endothelial dysfunction," <i>Circulation</i> , 101:948-954, 2000.
	C37	Teupe <i>et al.</i> , "Vascular gene transfer of phosphomimetic endothelial nitric oxide synthase (S1177D) using ultrasound-enhanced destruction of plasmid-loaded microbubbles improves vasoreactivity," <i>Circulation</i> , 105:1104-1109, 2002.
	C38	Torchilin <i>et al.</i> , "TAT peptide on the surface of liposomes affords their efficient intracellular delivery even at low temperature and in the presence of metabolic inhibitors," <i>Proc. Natl. Acad. Sci., USA</i> , 98:8786-8791, 2001.
	C39	Vallance <i>et al.</i> , "Nitric oxide--from mediator to medicines," <i>J. Royl. Coll. Physician London</i> , 28:209-219, 1994.
	C40	Venema <i>et al.</i> , "Role of the enzyme calmodulin-binding domain in membrane association and phospholipid inhibition of endothelial nitric oxide synthase," <i>Amer. Soc. Biochem. Molec. Biol.</i> , 270:14705-14711, 1995.
	C41	Woodman <i>et al.</i> , "Induction of nitric oxide synthase mRNA in coronary resistance arteries isolated from exercise-trained pigs," <i>Am. J. Physiol.</i> , 273(6pt2):H2575-2579, 1997.
	C42	Yang <i>et al.</i> , "Apolipoprotein B mRNA editing and the reduction in synthesis and secretion of the atherogenic risk factor, apolipoprotein B100 can be effectively targeted through TAT-mediated protein transduction," <i>Molec. Pharmacol.</i> , 61(2):269-276, 2002.
	C43	Yap <i>et al.</i> , "Distribution and function of recombinant endothelial nitric oxide synthase in transplanted hearts," <i>Cardiovascular Res.</i> , 42(3):720-722, 1999.

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January 12, 2005

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Steven L. Highlander

### MS AMENDMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 10/808,248 entitled "METHOD OF TREATMENT OF ENDOTHELIAL DYSFUNCTION AND ENGINEERED PROTEINS FOR SAME" – Elmer M. Price et al.*  
*Our reference: UVMO:024US*  
*Client reference: 02UMC062*

Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references C1-C43.

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/UVMO:024US.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

Steven L. Highlander  
Reg. No. 37,642

SLH/mar  
Encl: as noted